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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 175 and 176

[Docket No. 92F–0111]

Indirect Food Additives: Adhesives and Components of Coatings and Paper and Paperboard Components

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the food additive regulations to provide for the safe use of 2-acrylamido-2-methyl-propanesulfonic acid, homopolymer, sodium salt in food-contact adhesives and as a component of paper and paperboard intended to contact food. This action is in response to three petitions filed by The Lubrizol Corp.

DATES: This rule is effective [*insert date of publication in the* **Federal Register**]; Written objections and requests for a hearing by [*insert date 30 days after date of publication in the* **Federal Register**].

ADDRESSES: Submit written objections to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061 Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Edward J. Machuga, Center for Food Safety and Applied Nutrition (HFS–215), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202–418–3085.

SUPPLEMENTARY INFORMATION:

I. Background

In a notice published in the **Federal Register** of April 8, 1992 (57 FR 11958), FDA announced that three food additive petitions (FAP 9B4133, 9B4131, and 9B4132) had been filed on behalf of The Lubrizol Corp., 29400 Lakeland Blvd., Wickliffe, OH 44092–2298. The petitions proposed, respectively, that the food additive regulations in § 175.105 *Adhesives* (21 CFR 175.105), § 176.170 *Components of paper and paperboard in contact with aqueous and fatty foods* (21 CFR 176.170), and § 176.180 *Components of paper and paperboard in contact with dry food* (21 CFR 176.180) be amended to provide for the safe use of poly(sodium 2-acrylamido-2-methylpropanesulfonate) in adhesives and as components of paper and paperboard intended to contact food.

In the filing notice, FDA used the common name to identify the additive. However, in the final rule, the Chemical Abstract Service name, 2-acrylamido-2-methyl-propanesulfonic acid, homopolymer, sodium salt, is used because the structure of the food additive is more readily understood from this name. In addition, FDA believes that listing the additive under both §§ 176.170 and 176.180 is redundant because § 176.180(b)(1) (21 CFR 176.180(b)(1)) permits the use of those substances listed in § 176.170 (21 CFR 176.170) as components of paper and paperboard in contact with dry food. Therefore, FDA is listing the proposed uses of the additive only under §§ 176.170 and 175.105.

In FDA's evaluation of the safety of 2-acrylamido-2-methyl-propanesulfonic acid, homopolymer, sodium salt, the agency reviewed the safety of the additive itself and the chemical impurities that may be present in the additive resulting from its manufacturing process. Although the additive itself has not been shown to cause cancer, it may contain minute amounts of acrylamide and acrylonitrile as impurities resulting from its manufacture. These chemicals have been shown to cause cancer in test animals. Residual amounts of impurities are commonly found as constituents of chemical products, including food additives.

II. Determination of Safety

Under the general safety standard of the Federal Food, Drug, and Cosmetic Act (the act), (21 U.S.C. 348(c)(3)(A)), a food additive cannot be approved for a particular use unless a fair evaluation of the data available to FDA establishes that the additive is safe for that use. FDA's food additive regulations (21 CFR 170.3(i)) define safe as ''a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use.''

The food additives anticancer, or Delaney, clause of the act (21 U.S.C. 348(c)(3)(A)) provides that no food additive shall be deemed safe if it is found to induce cancer when ingested by man or animal. Importantly, however, the Delaney clause applies to the additive itself and not to impurities in the additive. That is, where an additive itself has not been shown to cause cancer, but contains a carcinogenic impurity, the additive is properly evaluated under the general safety standard using risk assessment procedures to determine whether there is a reasonable certainty that no harm will result from the intended use of the additive. *Scott* v. *FDA*, 728 F.2d 322 (6th Cir. 1984).

III. Safety of the Petitioned Uses of the Additive

FDA estimates that the petitioned uses of the additive, 2-acrylamido-2-methyl-propanesulfonic acid, homopolymer, sodium salt, will result in exposure to no greater than 100 parts per billion (ppb) of the additive in the daily diet (3 kilograms (kg)) or an estimated daily intake (EDI) of no more than 300 micrograms per person per day (μg/p/d)(Ref. 1).

FDA does not ordinarily consider chronic toxicological studies to be necessary to determine the safety of an additive whose use will result in such low exposure levels (Ref. 2), and the agency has not required such testing here. However, the agency has reviewed the available toxicological data on the additive and concludes that the estimated small dietary exposure resulting from the petitioned uses of this additive is safe.

FDA has evaluated the safety of this additive under the general safety standard, considering all available data and using risk assessment procedures to estimate the upper-bound limit of lifetime

human risk presented by acrylamide and acrylonitrile, the carcinogenic chemicals that may be present as impurities in the additive. The risk evaluation of acrylamide and acrylonitrile has two aspects: (1) Assessment of exposure to the impurities from the petitioned uses of the additive; and (2) extrapolation of the risk observed in the animal bioassays to the conditions of exposure to humans.

A. Acrylamide

FDA has estimated the exposure to acrylamide from the petitioned uses of the additive as a component of adhesives and of paper and paperboard in contact with food to be no more than 0.15 part per trillion (ppt) in the daily diet (3 kg), or 0.45 nanogram per person per day (ng/p/d) (Ref. 3). The agency used published data from a long-term rat bioassay on acrylamide conducted by Johnson et al. (Ref. 4), in addition to unpublished data from this bioassay contained in FAP 9B4131, to estimate the upper-bound limit of lifetime human risk from exposure to this chemical resulting from the petitioned uses of the additive. The authors reported that the test material caused significantly increased incidences of thyroid follicular adenomas and testicular mesotheliomas in male rats, and mammary tumors (adenomas or adenocarcinomas; fibromas or fibroadenomas; adenocarcinomas alone), central nervous system tumors (brain astrocytomas, brain or spinal cord glial tumors) and uterine tumors in female rats.

Based on the agency's estimate that exposure to acrylamide will not exceed 0.45 ng/p/d, FDA estimates that the upper-bound limit of lifetime human risk from the petitioned uses of the subject additive is 5.4×10^{-9}, or 5.4 in a billion (Refs. 5 and 6). Because of the numerous conservative assumptions used in calculating the exposure estimate, the actual lifetime-averaged individual exposure to acrylamide is likely to be substantially less than the estimated exposure, and therefore, the probable lifetime human risk would be less than the upper-bound limit of lifetime human risk. Thus, the agency concludes that there is reasonable certainty that no harm from exposure to acrylamide would result from the petitioned uses of the additive.

B. Acrylonitrile

FDA has estimated the exposure to acrylonitrile from the petitioned uses of the additive as a component of adhesives and of paper and paperboard in contact with food to be no more than 0.3 ppt in the daily diet (3 kg), or 0.9 ng/p/d (Ref. 3). The agency used data from a long-term rodent bioassay on acrylonitrile conducted by Quast et al. (Ref. 7), to estimate the upper-bound limit of lifetime human risk from exposure to this chemical resulting from the petitioned uses of the additive. The authors reported that the test material caused astrocytomas of the nervous system, papillomas and carcinomas of the tongue, papillomas and carcinomas of the stomach, and Zymbal's gland carcinomas in male and female rats. The authors also reported carcinomas of the small intestine and the mammary gland in female rats.

Based on the agency's estimate that exposure to acrylonitrile will not exceed 0.9 ng/p/d, FDA estimates that the upper-bound limit of lifetime human risk from the petitioned uses of the subject additive is 1.6×10^{-9}, or 1.6 in a billion (Refs. 8 and 9). Because of the numerous conservative assumptions used in calculating the exposure estimate, the actual lifetime-averaged individual exposure to acrylonitrile is likely to be substantially less than the estimated exposure, and therefore, the probable lifetime human risk would be less than the upper-bound limit of lifetime human risk. Thus, the agency concludes that there is reasonable certainty that no harm from exposure to acrylonitrile would result from the petitioned uses of the additive.

C. Need for Specifications

The agency has also considered whether specifications are necessary to control the amount of acrylamide and acrylonitrile as impurities in the food additive. The agency finds that specifications are not necessary for the following reasons: (1) Because of the low levels at which acrylamide and acrylonitrile may be expected to remain as impurities following production of the additive, the agency would not expect these impurities to become components of food at other than extremely low levels; and (2) the upper-bound limits of lifetime human risk from exposure to acrylamide and acrylonitrile are very low, 5.4 in a billion and 1.6 in a billion, respectively.

IV. Conclusion

FDA has evaluated data in the three petitions and other relevant material. Based on this information, the agency concludes that: (1) The proposed uses of the additive as a component of adhesives, and paper and paperboard in contact with food are safe, (2) the additive will achieve its intended technical effect, and therefore, (3) the regulations in §§ 175.105 and 176.170 should be amended as set forth below.

In accordance with § 171.1(h) (21 CFR 171.1(h)), the petition and the documents that FDA considered and relied upon in reaching its decision to approve the petition are available for inspection at the Center for Food Safety and Applied Nutrition by appointment with the information contact person listed above. As provided in § 171.1(h), the agency will delete from the documents any materials that are not available for public disclosure before making the documents available for inspection.

V. Environmental Impact

The agency has determined under 21 CFR 25.32(i) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VI. Paperwork Reduction Act of 1995

This final rule contains no collection of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

VII. Objections

Any person who will be adversely affected by this regulation may at any time on or before [*insert date 30 days after date of publication in the* **Federal Register**] file with the Dockets Management Branch (address above) written objections thereto. Each objection shall be separately numbered, and each numbered objection shall specify with particularity the provisions of the regulation to which objection is made and the grounds for the objection. Each numbered objection

on which a hearing is requested shall specifically so state. Failure to request a hearing for any particular objection shall constitute a waiver of the right to a hearing on that objection. Each numbered objection for which a hearing is requested shall include a detailed description and analysis of the specific factual information intended to be presented in support of the objection in the event that a hearing is held. Failure to include such a description and analysis for any particular objection shall constitute a waiver of the right to a hearing on the objection. Three copies of all documents shall be submitted and shall be identified with the docket number found in brackets in the heading of this document. Any objections received in response to the regulation may be seen in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

VIII. References

The following references have been placed on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Memorandum of an internal communication between A. B. Bailey, Chemistry and Environmental Review Team, K. Biddle and K. P. Misra, Division of Health Effects Evaluation, and D. N. Harrison, Division of Petition Control, dated October 6, 1998.

2. Kokoski, C. J., ''Regulatory Food Additive Toxicology,'' In *Chemical Safety Regulation and Compliance*, edited by F. Homburger, and J. K. Marquis, New York, NY, pp. 24–33, 1985.

3. Memorandum dated June 15, 1998, from Chemistry and Environmental Review Team to the Division of Petition Control, ''Use of poly(sodium 2-acrylamido-2-methylpropanesulfonate) in Latex Emulsions for Adhesives and Coatings in Paper and Paperboard.''

4. Johnson, K. A., Gorzinski, S. J., Bodner, K. M., Campbell, R. A., Wolf, C. H., Friedman, M. A., and Mast, R. W. ''Chronic Toxicity and Oncogenicity Study on Acrylamide Incorporated in the Drinking Water of Fischer 344 rats,'' *Toxicology and Applied Pharmacology*, 85:154–168, 1986.

5. Memorandum dated December 18, 1998, from the Division of Petition Control to the Quantitative Risk assessment Committee, ''Estimation of Upper-Bound Lifetime Risk for 2-acrylamido-2-methylpropanesulfonic acid, homopolymer, sodium salt, FAPS 9B4131, 9B4132 and 9B4133.''

6. Memorandum of Conference, Date: February 13, 1985; June 6, 1985; May 31, 1996, Place: FDA, CFSAN, Washington, DC, Purpose: Cancer Assessment Committee Meeting, Subject: Acrylamide.

7. Quast, J. F., Wade, C. E., Humiston, C. G., Carreon, R. M., Hermann, E. A., Park, C. N., Schwetz, B. A. ''A Two Year Toxicity and Oncogenicity Study with Acrylonitrile Incorporated in the Drinking Water of Rats,'' Toxicology Research Laboratory, Health and Environmental Sciences, Dow Chemical USA, Midland, MI 48640. Final report dated January 22, 1980. Corrections dated November 17, 1980.

8. Memorandum dated September 4, 1998, from the Division of Health Effects Evaluation to the Division of Petition Control, ''FAPs 9B4131, 9B4132, and 9B4133: Worst-Case Cancer Risk Assessment for Acrylonitrile,'' Correction to July 28, 1998, memorandum from the Division of Health Effects Evaluation to the Quantitative Risk Assessment Committee.

9. Memorandum dated July 28, 1998, from the Division of Health Effects Evaluation to the Quantitative Risk Assessment Committee, ''FAPs 9B4131, 9B4132, and 9B4133: Worst-Case Cancer Risk Assessment for Acrylonitrile'' and the April 15, 1999, Addendum.

List of Subjects

21 CFR Part 175

Adhesives, Food additives, Food packaging.

21 CFR Part 176

Food additives, Food packaging.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR parts 175 and 176 are amended as follows:

PART 175—INDIRECT FOOD ADDITIVES: ADHESIVES AND COMPONENTS OF COATINGS

1. The authority citation for 21 CFR part 175 continues to read as follows:

Authority: 21 U.S.C. 321, 342, 348, 379e.

2. Section 175.105 is amended in the table in paragraph (c)(5) by alphabetically adding a new entry under the heading ''Substances'' to read as follows:

§ 175.105 Adhesives.

* * * * *

(c) * * *

(5) * * *

Substances	Limitations
* * * *	* * *
2-Acrylamido-2-methyl-propanesulfonic acid, homopolymer, sodium salt (CAS Reg. No. 35641–59–9).	
* * * *	* * *

PART 176—INDIRECT FOOD ADDITIVES: PAPER AND PAPERBOARD COMPONENTS

3. The authority citation for 21 CFR part 176 continues to read as follows:

Authority: 21 U.S.C. 321, 342, 346, 348, 379e.

4. Section 176.170 is amended in the table in paragraph (b)(2) by alphabetically adding a new entry under the headings ''List of substances'' and ''Limitations'' to read as follows:

§ 176.170 Components of paper and paperboard in contact with aqueous and fatty foods.

* * * * *

(b) * * *

(2) * * *

List of Substances	Limitations
* * * *	* * *
2-Acrylamido-2-methyl-propanesulfonic acid, homopolymer, sodium salt (CAS Reg. No. 35641–59–9).	For use only in coatings at a level not to exceed 0.01 mg/in^2
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Dated: 2/8/00
February 8, 2000

CERTIFIED TO BE A TRUE COPY OF THE ORIGINAL

Margaret M. Dotzel
Acting Associate Commissioner for Policy

[FR Doc. 99–???? Filed ??–??–99; 8:45 am]

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